

REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow. Claims 1, 22, 33, and 38 have been amended. No claims have been cancelled. Claim 45 has been added. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, an appropriate defined status identifier. Thus, claims 1-17, 22-34, and 36-45 remain pending in the application. Support new claim 45 can be found in paragraph [0024] of the specification.

Claim Rejections - 35 USC § 112/New Matter

Claims 22-32, 38-42 and 44 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for allegedly introducing new matter. Specifically, claims 22-32, 41, and 42 were rejected because the specification allegedly did not teach “applying pre-made aggregates of metallic colloids or nanoparticles to the probe-target complex.” Claims 38-40 were rejected because the specification allegedly did not teach “a Raman tag attached to the backbone of the at least one of the Raman-active oligonucleotide probes.” Applicants respectfully traverse these rejections.

Step c) of independent claim 22 has been amended to recite “aggregating metal colloids or nanoparticles with the probe-target complex in the presence of a mono-valent salt, wherein the metal colloids are pre-made.” Support for this amendment can be found in paragraph [0050] of the specification. Although Applicants believe that the language in the previous amendment was fully supported by the specification, the current language more closely follows the language of paragraph

[0050]. Applicants submit that Amended claim 22 does not introduce any new matter and respectfully requests withdrawal of the rejection.

Claim 38 has been amended to remove “backbone” although Applicants disagree with the Examiner’s characterization of Figure 4b. Figure 4b illustrates AmC6 labels attached to both ends (5NGT3N), one end (GT3N), and the middle (i.e., the backbone) (GTMN) of the nucleotide probe. Applicants submit that the current amendment claim 38 removes any alleged new matter and respectfully requests withdrawal of the rejection.

Claim Rejections - 35 USC § 112

Claims 22-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the phrase “the affect of the first probe on the second probe” in step d) of claim 22 was found unclear. Also, the phrase “pre-made aggregates of metallic colloids or nanoparticles” was found to unclear a whether pre-made applied only to the metallic colloids or both the metallic colloids and nanoparticles. Applicant respectfully traverse these rejections.

The word “probe” in step d) of claim 22 was amended to “label.” Step d) is now consistent with step a). Step a) introduced a first label and a second label, the first label affecting the Raman spectra or fluorescent signal of the second label. Applicants submit that amended step d) of claim 22 is definite and respectfully request withdrawal of the rejection.

Step c) of claim 22 has been amended to clarify that “the metal colloids are pre-made.” Applicants submit that amended step c) of claim 22 is definite and respectfully request withdrawal of the rejection.

Claim Rejections - 35 USC § 102

Claims 1-2, 5-7, 9, 13-17, 37, 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Cao et al. (Science August 2002 vol. 297 p. 1536) as evidenced by Faulds et al. (Talanta 2005 vol. 67 p. 667). Applicants respectfully traverse this rejection.

“A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Verdegall Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Independent claim 1 has been amended to include the limitation that the positively charged Raman signal enhancer maintains its positive charge after binding with the probe-target complex. As discussed in more detail in the declaration of Dr. Xing Su attached herewith, the Cy3 labeled probe taught by Cao cannot maintain a positive charge after binding with the probe-target complex. Cao teaches probe consisting of an alkylthiol-capped oligonucleotide strand with a Cy3 label attached to a gold nanoparticle. (p.1537, col. 1; Fig. 1). Indeed the Cy3 enhancer of the probe taught by Cao loses its charge as soon as the amine nitrogen of the Cy3 label binds to the gold nanoparticle. Thus, the probe and the method of Cao do not anticipate independent claim 1 or any of the claims that depend from claim 1.

Claim Rejections - 35 USC § 103

Claims 3-4, 8 are rejected under 35 U.S.C. 103(a) as being over Cao et al. (Science August 2005 Vol 297 p. 1536) in view of Mirkin et al. (US Patent 6361944 March 26, 2002) as evidenced by Faulds et al. (Talanta 2005 vol. 67 p. 667). Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cao et al. (Science August 2002 Vol 297 p. 1536) in view of Pastinen et al. (Genome Research July 2000 Vol. 10(7) p. 1031) as evidenced by Faulds et al. (Talanta 2005 vol.

67 p. 667). Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cao et al (Science August 2002 Vol 297 p. 1536) in view of Lane et al. (US Patent 5,770,365 June 23, 1998) as evidenced by Faulds et al. (Talanta 2005 vol. 67 p. 667). Claims 22-24, 26-27, and 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cao et al (Science August 2002 Vol 297 p. 1536) in view of Chan et al. (US Patent Application Publication March 27, 2003) and Corbierre et al. (Journal of American Chem. Soc 2001 Vol. 123 p. 10411) as evidenced by Faulds et al (Talanta 2005 vol. 67 p. 667). Claim 25 is being rejected under 35 U.S.C. 103(a) as being unpatentable over Cao et al (Science August 2002 Vol 297 p. 1536) in view of Chan et al. (US Patent Application Publication March 27, 2003) as evidenced by Faulds et al (Talanta 2005 vol. 67 p. 667) as applied to 22-24, 26-27, and 29-32 above and further in view of Bruchez, Jr. et al. (US Patent Application 09/815585 March 21, 2002). Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cao et al (Science August 2002 Vol 297 p. 1536) in view of Chan et al. (US Patent Application Publication March 27, 2003) as evidenced by Faulds et al (Talanta 2005 vol. 67 p. 667) as applied to 22-24, 26-27, and 29-32 above and further in view of Livak et al. (US Patent 5,723,591 March 3, 1998). Claims 33, 39, and 43 are rejected under 35 U.S.C. 103(a) as being over Cao et al. (Science August 2002 Vol 297 p. 1536) in view of Garimella et al. (US Patent Application Publication 2003/0082588 May 1, 2003) as evidenced by Faulds et al. (Talanta 2005 vol. 67 p. 667). Claims 34, 36, and 40 are rejected under under 35 U.S.C. 103(a) as being over Cao et al. (Science August 2002 Vol 297 p. 1536) in view of Garimella et al. (US Patent Application Publication 2003/0082588 May 1, 2003) as applied to Claims 33, 39, and 43 and further in view of Mirkin et al. (US Patent 6361944 March 26, 2002). Claims 41-42 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cao et al. (Science August 2002 Vol 297 p. 1536) in view

of Corbierre et al. (Journal of American Chem. Soc 2001 Vol. 123 p. 10411) as evidenced by Faulds et al (Talanta 2005 vol. 67 p. 667).

Independent claims 1 and 33 have been amended to include the limitation that the positively charged Raman signal enhancer maintains its positive charge after binding with the probe-target complex. This feature is neither taught nor suggested by any of the applied references. Therefore any combination of the applied references lacks at least one claimed feature of independent claims 1 and 33. Therefore no combination of the applied references renders independent claims 1 and 33 or any of the claims that depend on these claims obvious. Applicants respectfully request withdrawal of the rejections.

Independent claim 22 recites that “the first label affecting the Raman spectra or fluorescent signal generated by the second label based on the orientation of the first label to the second label.” Chan teaches several detections systems, including FRET (in which electrons from a donor label molecule transfer to an acceptor label molecule, resulting in a detectable change in signal). (Chan paragraph [0148]) However, neither Chan, nor any other of the cited references teach or suggest a first label affecting the Raman spectra or fluorescent signal generated by the second label based on a change in the orientation of a label. No combination of the applied references teaches all of the claimed limitations of claim 22. Therefore, no combination of the applied references render claim 22 obvious or any of the claims that depend from claim 22.

New Claim 45

Regarding new claim 45, the Cy3 Raman dye disclosed by Cao operates by way of an amine nitrogen. Amended new claim 45 excludes the heteroatoms taught by Cao. Applicants note that the use of a negative limitation to exclude prior art is a practice accepted by the USPTO and the courts.

See MPEP 2173.05(i); *In re Wakefield*, 422 F.2d 897 (CCPA 1970). Further, if alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. See *In re Johnson*, 558 F.2d 1008, 1019 (CCPA 1977)("[the] specification, having described the whole, necessarily described the part remaining.").

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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